

Systematic review and meta-analysis of Internet interventions for smoking cessation among adults

Amanda L Graham^{1,2}
 Kelly M Carpenter³
 Sarah Cha¹
 Sam Cole³
 Megan A Jacobs¹
 Margaret Raskob³
 Heather Cole-Lewis^{4,5}

¹Schroeder Institute for Tobacco Research and Policy Studies, Truth Initiative, Washington, DC, ²Department of Oncology, Georgetown University Medical Center/Cancer Prevention and Control Program, Lombardi Comprehensive Cancer Center, Washington, DC, ³Alere Wellbeing, Seattle, WA, ⁴Johnson & Johnson Health and Wellness Solutions, Inc., New Brunswick, NJ, ⁵ICF International, Rockville, MD, USA

Background: The aim of this systematic review was to determine the effectiveness of Internet interventions in promoting smoking cessation among adult tobacco users relative to other forms of intervention recommended in treatment guidelines.

Methods: This review followed Cochrane Collaboration guidelines for systematic reviews. Combinations of “Internet,” “web-based,” and “smoking cessation intervention” and related keywords were used in both automated and manual searches. We included randomized trials published from January 1990 through to April 2015. A modified version of the Cochrane risk of bias assessment tool was used. We calculated risk ratios (RRs) for each study. Meta-analysis was conducted using random-effects method to pool RRs. Presentation of results follows the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines.

Results: Forty randomized trials involving 98,530 participants were included. Most trials had a low risk of bias in most domains. Pooled results comparing Internet interventions to assessment-only/waitlist control were significant (RR 1.60, 95% confidence interval [CI] 1.15–2.21, $I^2=51.7\%$; four studies). Pooled results of largely static Internet interventions compared to print materials were not significant (RR 0.83, 95% CI 0.63–1.10, $I^2=0\%$; two studies), whereas comparisons of interactive Internet interventions to print materials were significant (RR 2.10, 95% CI 1.25–3.52, $I^2=41.6\%$; two studies). No significant effects were observed in pooled results of Internet interventions compared to face-to-face counseling (RR 1.35, 95% CI 0.97–1.87, $I^2=0\%$; four studies) or to telephone counseling (RR 0.95, 95% CI 0.79–1.13, $I^2=0\%$; two studies). The majority of trials compared different Internet interventions; pooled results from 15 such trials (24 comparisons) found a significant effect in favor of experimental Internet interventions (RR 1.16, 95% CI 1.03–1.31, $I^2=76.7\%$).

Conclusion: Internet interventions are superior to other broad reach cessation interventions (ie, print materials), equivalent to other currently recommended treatment modes (telephone and in-person counseling), and they have an important role to play in the arsenal of tobacco-dependence treatments.

Keywords: systematic review, meta-analysis, Internet, smoking cessation, tobacco control

Correspondence: Amanda L Graham
 Schroeder Institute for Tobacco Research and Policy Studies, Truth Initiative, 900 G Street NW, Fourth Floor, Washington, DC 20001, USA
 Tel +1 202 454 5938
 Fax +1 202 454 5785
 Email agraham@truthinitiative.org

Background

Health care around the globe is being transformed to deliver care and services in ways that are less costly and more convenient for both providers and patients.^{1,2} At the center of this transformation are digital health interventions facilitated by the Internet. Internet interventions can reach large numbers of people who may not otherwise access preventive and clinical health care services and engage them with convenient, accessible,



multimedia interventions that can be used flexibly, often anonymously, for as long as the user desires.³ Personalized and individually tailored treatment can be delivered via the Internet in ways that mimic many of the aspects of face-to-face clinical interventions.⁴ Importantly, whereas ongoing clinical intervention within the health care delivery system is often prohibitively expensive and unsustainable, treatment via Internet interventions is scalable, sustainable, and cost-efficient.⁵

Internet interventions for tobacco cessation may have an important role to play in improving individual, community, and population health. Tobacco use remains the leading cause of preventable death worldwide.⁶ It is widely accepted that comprehensive tobacco control measures are needed to reduce tobacco use, including efforts to provide tobacco-dependence treatments on a population-wide basis.⁷ Cessation treatment guidelines recommend screening for tobacco use in health care settings, behavioral counseling delivered via individual, group, or telephone counseling, and pharmacotherapy.⁸⁻¹⁰ However, these approaches may not reach a majority of smokers. For example, in the USA, only 20.9% of tobacco users are counseled about tobacco use and only 7.6% are advised to use pharmacotherapy by a health care provider.¹¹ Residents throughout the USA and Canada have access to quitline services, but uptake is <10% of smokers each year.¹² The use of cessation medication widely varies even when it is free or inexpensive to access.¹³⁻¹⁶ To curb the tobacco use epidemic and avert the enormous toll projected from tobacco, additional interventions are needed to complement the existing arsenal of tobacco treatment strategies.

Internet interventions for smoking cessation are currently offered around the world by a broad range of national, regional, and local government entities, as well as commercial and nonprofit organizations.¹⁷ Hundreds of thousands of smokers register on web-based cessation programs each year, whether through programs offered by quitlines,¹⁸ employers, and health plans,¹⁹ or on publicly available, high-volume web-based cessation programs around the globe.²⁰⁻²² The Internet is the first place many people turn to for information and assistance with health-related concerns,²³ and it has been estimated that millions of smokers look online for quit smoking assistance each year.^{24,25}

However, despite the provision of Internet cessation interventions by a broad range of stakeholders around the globe, and the demonstrated uptake of Internet cessation interventions among smokers, tobacco-dependence treatment guidelines have noted their promise but have stopped short

of including them as a recommended treatment strategy, instead calling for more research on their effectiveness.^{8-10,26} A recent review of reviews conducted by Patnode et al⁹ considered evidence from six systematic reviews, drawing primarily on the most recent 2013 review by Civljak et al.²⁷ They concluded that Internet-based behavioral interventions for smoking cessation have high potential applicability to primary care within the USA but that evidence on the use of Internet interventions was limited and not definitive.

The objective of this systematic review was to determine the effectiveness of Internet interventions in promoting smoking cessation among adult tobacco users, considering the numerous studies published since the 2013 review by Civljak et al.²⁷ We were particularly interested in studies comparing Internet interventions to other forms of treatment that have been recommended in treatment guidelines to better understand whether there is a role in comprehensive tobacco control for Internet-based approaches. We examined whether Internet interventions are more effective in promoting abstinence compared to: 1) assessment-only/waitlist control, 2) print materials, 3) face-to-face counseling, 4) telephone counseling, and 5) static/generic websites.

Methods

Design

This study is a systematic review of randomized controlled trials following Cochrane methodological guidance.²⁸ The PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) checklist and flow diagram are used as aids in the reporting of this systematic review. A structured approach was used to build the eligibility criteria.²⁹

Eligibility criteria

Participants: We included studies conducted with adults aged ≥ 18 years regardless of sex; studies with children were included, provided that outcome data for adults were reported separately. We included studies that involved participants who were current smokers at the outset of the trial. We included studies with recent quitters as long as abstinence was reported for current smokers. Smokeless tobacco studies were excluded.

Interventions: For the purposes of this review and borrowing from published definitions, we define Internet smoking cessation interventions as being primarily composed of directive information and support services delivered via the Internet with the goal of supporting the user in trying to quit tobacco.³⁰ Internet interventions are largely self-guided, at least partially automated, and take advantage of the

interactive nature of the Internet.³¹ The basis of such programs is typically behaviorally or cognitive-behaviorally based treatments that have been operationalized and transformed for delivery via the Internet.³² For the purposes of this review, we exclude mHealth interventions, such as text messaging or interventions delivered solely through a mobile device.³³ mHealth interventions were excluded in order to decrease heterogeneity in the interventions assessed in this review and to be consistent with previous reviews of Internet interventions. Nonetheless, excluding interventions delivered solely through a mobile device does not exclude Internet smoking cessation interventions that may have been accessed through a mobile web browser.

Comparisons: There were no exclusion criteria for comparison interventions.

Outcomes: Studies that reported abstinence from smoking with at least a 1-month follow-up as the primary outcome were included. Measures of abstinence included 7-day point prevalence abstinence, 30-day point prevalence abstinence, repeated point abstinence, continuous abstinence, sustained abstinence, and prolonged abstinence. Self-reported and biochemically verified metrics of abstinence were included.

Report characteristics and study design: We included English-language quantitative studies that employed a randomized design published since 1990. We excluded cohort studies, qualitative studies, editorials, letters, and commentaries, studies where we could not identify a full text, and articles that did not report the minimum information required.

Information sources and search strategy

We employed a mixed automated and manual search strategy. We conducted a comprehensive literature search using the following bibliographic databases: PubMed, CINAHL Plus with Full Text, Cochrane Library, PsycINFO, EMBASE, Web of Science, Communication and Mass Media Complete, Global Health, Grey Literature Report, IEEE Xplore, and Google Scholar. We used a combination of the constructs “Internet,” “web-based,” and “smoking cessation intervention” and related keywords to ensure broad coverage of published studies. Search terms were intentionally broad to ensure that all relevant articles would be captured ([Supplementary materials, Appendix 1](#)). Our search covered English language papers published between January 1990 and April 2015. We also reviewed the reference lists of included manuscripts and previous systematic reviews. All other databases were searched with free text terms reflecting inclusion criteria. Citations were compiled in EndNote (EndNote Version X6;

Thomson Reuters, Philadelphia, PA, USA) and imported and de-duplicated in EPPI-Reviewer 4.0 (University College London, Institute of Education, University of London, UK).³⁴

Study selection

The title and abstract of identified citations were screened for eligibility by two reviewers. Items were included at this stage if they appeared to meet inclusion criteria based on information in the title and abstract and were excluded only if clearly ineligible. When only the study title was available, the presence of keywords in the title related to “an Internet intervention” and “smoking cessation” warranted full-text review. Next, we obtained the full texts of citations considered as potentially eligible. Two reviewers independently screened the full text for eligibility using a standardized and pilot-tested screening process. Discrepancies were resolved by the team. Finally, reference lists of previous reviews and recent publications were checked.

Data collection process and data items

Eligible studies were coded to capture both substantive and methodological characteristics. The coding focused on the following features of the studies: identifying information, funding source, design, aims and objectives, variables related to the characteristics of participants, the nature of the intervention and its implementation, the nature of the comparison condition(s) and their implementation, analytical methods, follow-up duration and rates, and outcome measurements. In addition, we extracted information about strategies used to promote engagement/adherence in accordance with the study by Alkhalidi et al.³⁵ We included selected items from the CONSORT-EHEALTH checklist relevant to the reporting of eHealth trials³⁶ (eg, intervention access, level of human involvement, and engagement strategies).

The data abstraction form was pilot tested on a purposive sample of eligible studies.^{22,37–41} Reviewers were retrained on coding items that showed discrepancies during this process, and the coding scheme was adapted. This process was repeated until a high level of consistency was achieved. The remaining studies were coded by a single reviewer and reviewed by a second reviewer. Discrepancies were resolved by group discussion.

Risk of bias in individual studies

We used the Cochrane Collaboration tool for assessing the risk of bias.²⁸ As in the systematic review by Mathieu et al,⁴² we elected not to consider reporting bias since few studies prospectively registered their protocols. Following

Civiljak et al,²⁷ we did not assess participant blinding due to the inherent difficulty in blinding participants to behavioral interventions. Reviewers' judgments regarding the risk of bias for each criterion were rated as low, high, or unclear. We computed graphic representations of potential bias within and across studies using EPPI-Reviewer 4.0 software.

Data analysis

The majority of studies reported cessation outcomes at multiple endpoints using multiple metrics (eg, 7-day abstinence, 30-day abstinence). When the authors specified a primary outcome (eg, used for power analyses), we selected it for analysis; if a primary outcome was not explicitly stated, we included the longest endpoint and most conservative metric of abstinence. We conducted an intention-to-treat (ITT) analysis, including all participants as randomized in the denominator; individuals lost to follow-up were counted as smokers. Abstinence rates were summarized as risk ratios (RRs) and 95% confidence intervals (CIs) using the ITT principle, which were calculated as: $(\text{number of quitters: intervention arm}) / (\text{number randomized: intervention arm}) / ((\text{number of quitters: control arm}) / (\text{number randomized: control arm}))$. We display descriptive data alongside RRs with 95% CIs in forest plots.

We assessed statistical heterogeneity using the I^2 statistic, which assesses the proportion of the variation between studies due to heterogeneity rather than to chance.⁴³ I^2 ranges from 0% to 100%, with 0% indicating no observed heterogeneity and larger values showing increasing heterogeneity. The importance of the observed value of I^2 depends on the magnitude and direction of effects as well as the strength of evidence for heterogeneity (eg, P -value from the chi-squared test). I^2 values of 25%, 50%, and 75% approximately correspond to low, moderate, and high levels of statistical heterogeneity, respectively.⁴³

We judged random-effects meta-analysis to be appropriate for all five comparisons of interest. In each of these comparisons, we pooled the weighted average of RRs using a random-effects model and 95% CI. To be conservative, we excluded trials with less than a 3-month follow-up, those that were feasibility studies, and those with very low follow-up rates.

Results

Study selection

Figure 1 shows the study flow. A total of 80 records were reviewed for eligibility, and 37 were excluded ([Supplementary materials, Appendix 2](#)) for the following reasons: full text was not available ($n=3$), intervention did not meet

the definition of "Internet-based" ($n=9$), record was not a published study ($n=2$), not a randomized design ($n=11$), secondary analysis of outcome data presented elsewhere ($n=2$), smoking outcomes not reported ($n=8$), and we were unable to calculate abstinence rates using available data ($n=2$). Forty individual trials with a total of 98,530 participants were included (described in 43 reports) and are listed in [Supplementary materials \(Appendix 3\)](#).

Risk of bias within and across studies

Overall, the studies included in this review had low risk of bias in most or all areas assessed. Figure 2A displays the risk of bias summary for individual studies, and Figure 2B displays the risk of bias graph. Details regarding the assessment of risk for each individual study are noted in [Supplementary materials \(Appendix 4\)](#).

Selection bias: Most studies used an automated randomization strategy that was considered low risk. Allocation concealment was not often described, but when studies were automated, we judged allocation concealment bias risk as low. There was a higher risk when personnel were involved in randomization and allocation. For example, Emmons et al⁴⁴ used personnel to randomize the participants and allocation concealment was not described. The study by Haug et al⁴⁵ was conducted in inpatient rehabilitation centers, and participants were randomized by the week of their admission. We judged there to be a risk of selection bias since personnel would know ahead of time which participants would be in each group. Similarly, the study by Shuter et al⁴⁶ was judged to be at high risk since clinic personnel were involved in allocation and were not blinded.

Performance and detection bias: We evaluated the included studies with regard to personnel and their ability to influence outcomes and found most studies to be at low risk for performance bias. Most studies were conducted on the Internet with no personnel involvement in the delivery of the intervention. When personnel did have opportunities to influence participants (eg, in a clinic setting), risk was judged as unclear when interactions with personnel were not described. There were two trials in which performance bias was judged as high risk. In the study by Swan et al,⁴⁷ quitline counselors were not blind to condition but interacted with all participants. The study by Mehring et al⁴⁸ was also judged to be at high risk for performance bias as unblinded personnel interacted with all participants. Most trials conducted outcome assessments via the Internet with no risk of detection bias. Some trials, however, had assessors to collect the outcome data by phone for at least some participants. A few studies did not describe their assessors as blinded, leading

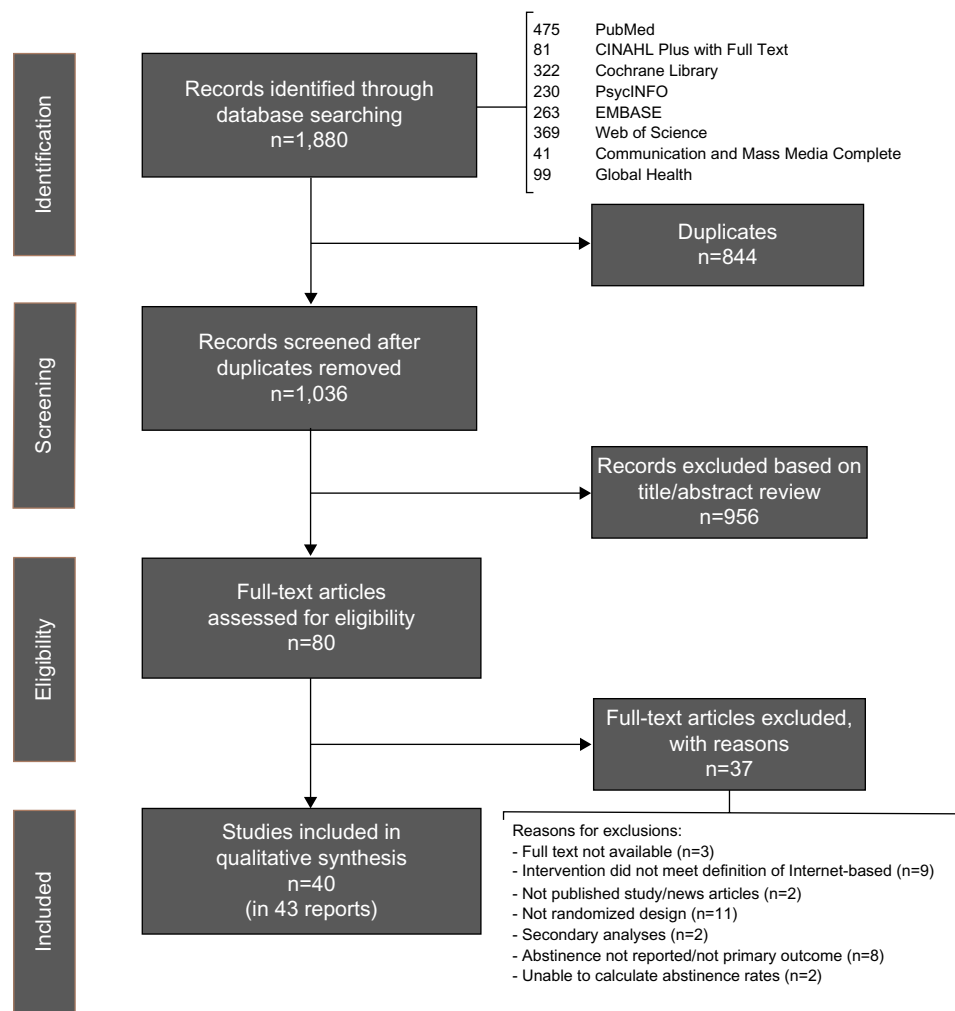


Figure 1 PRISMA flow diagram.

Abbreviation: PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

to ratings of unclear bias. No studies were believed to be at high risk of detection bias.

Attrition bias: Attrition is a particular challenge in web-based studies.⁴⁹ We focused on two elements when rating attrition bias: reporting outcomes and differential attrition by study arm. Reporting results with all randomized participants included and missing participants identified as smoking can protect against an overly optimistic interpretation of study findings that can occur when only responders are considered. With the exception of the studies by Bricker et al⁵⁰ and Humfleet et al,⁵¹ all studies provided this type of ITT analysis. Only half of included studies reported significance testing of attrition rates. Studies that did not report attrition by study arm or that did not report whether significance testing of attrition rates across arms was conducted were rated as unclear with regard to attrition bias^{37,38,51–60} unless they had very high follow-up rates (eg, 96% and 99% follow-up in the study by Shuter et al).⁴⁶ Studies that reported significantly different attrition rates across

arms were judged as high risk.^{48,61–65} Studies with low follow-up rates but equivalent attrition across study arms were not rated as high risk, as has been done in previous reviews.²⁷ Attrition varied greatly from study to study, with follow-up rates ranging from >95% in the study by Shuter et al⁴⁶ to follow-up rates approximately 5% in Mañanes and Vallejo.⁶⁴

Study characteristics

[Supplementary materials \(Appendix 4\)](#) details the characteristics of included studies with regard to participants, interventions, comparison, outcomes, study design, risk of bias notations, and other characteristics relevant to this review.

Recruitment strategies

Most studies recruited participants via the Internet using a variety of strategies, including search engine advertising,^{37,53,55,66–68} online ads,^{39,50,55,59,62,69–71} and social media.^{39,50} Five trials recruited new registered users on the website being evaluated.^{38,56,63,64,72}

A

| Studies | Random sequence allocation (selection bias) | Allocation concealment (selection bias) | Blinding of personnel (performance bias) | Blinding of outcome assessment (detection bias) | Incomplete outcome data (attrition bias) |
|---|---|---|--|---|--|
| An et al ⁷⁸ | + | + | + | + | + |
| An et al ⁴⁰ | + | + | + | ? | + |
| Berg et al ⁸¹ | + | + | + | + | - |
| Borland et al ⁷⁵ | + | + | + | ? | + |
| Brendryen et al ⁶⁹ | + | + | + | + | + |
| Brendryen and Kraft ¹⁰ | + | + | + | + | + |
| Bricker et al ⁹⁰ | + | + | + | + | + |
| Choi et al ⁵⁷ | + | ? | + | + | ? |
| Dezee et al ⁵⁸ | + | + | + | + | ? |
| Efveddali et al ⁶² | + | + | + | + | - |
| Emmons et al ⁴⁴ | + | ? | + | ? | + |
| Etter ⁸³ | + | + | + | + | - |
| Fraser et al ³⁸ | ? | ? | + | + | ? |
| Graham et al ⁶⁶ | + | ? | + | + | + |
| Haug et al ⁴⁵ | ? | - | + | ? | + |
| Herbec et al ⁵⁹ | + | + | + | + | ? |
| Humfleet et al ⁵¹ | + | ? | ? | ? | ? |
| Japuntich et al ⁵² | ? | ? | + | + | ? |
| Leykin et al ⁵³ | + | + | + | + | ? |
| Mañanes and Vallejo ⁶⁴ | + | + | + | + | - |
| Mason et al ⁷² | + | + | + | + | + |
| McClure et al ⁴⁹ | + | + | + | + | ? |
| McDonnell et al ⁸⁵ | + | + | + | + | ? |
| McKay et al ⁸⁷ | + | + | + | ? | ? |
| Mehring et al ⁴⁸ | + | ? | - | + | - |
| Muñoz et al ¹⁷ – Studies 3 and 4 | + | + | + | ? | ? |
| Muñoz et al ⁶⁸ | + | + | + | + | + |
| Oenema et al ⁶⁵ | + | + | + | + | - |
| Pisinger et al ⁶⁰ | + | + | ? | ? | ? |
| Rabius et al ⁵¹ | + | + | + | ? | + |
| Shuter et al ⁴⁶ | + | - | ? | ? | + |
| Simmons et al ⁷⁶ | + | + | ? | ? | ? |
| Smit et al ³⁹ | + | + | + | + | + |
| Stanczyk et al ⁷⁴ | + | + | + | ? | + |
| Stoddard et al ⁷⁷ | + | + | + | + | + |
| Strecher et al ⁵⁶ | + | + | + | + | ? |
| Strecher et al ⁴¹ | + | + | + | ? | + |
| Swan et al ⁴⁷ | + | + | - | + | + |
| Swartz et al ⁷³ | + | + | + | + | + |
| Wangberg et al ⁶² | + | + | + | + | + |

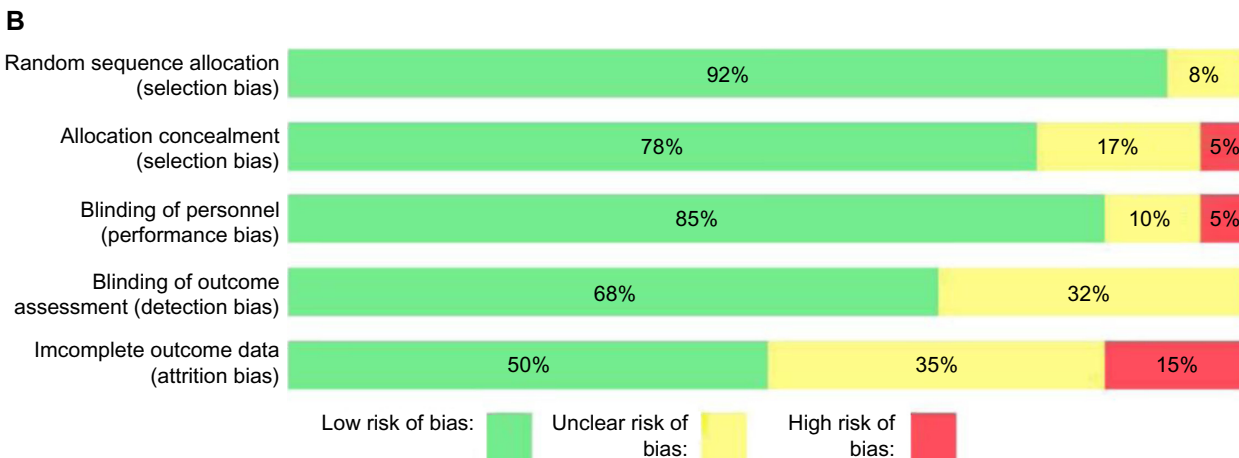


Figure 2 (A) Risk of bias summary; **(B)** risk of bias graph. **Notes:** “+” = low risk of bias; “-” = high risk of bias; “?” = unclear risk of bias.

Other reactive recruitment sources included newspapers and magazines,^{39,47,52,62} print advertisements such as flyers, posters, and billboards,^{52,62,73} radio and television advertisements,^{39,50,52} and other paid advertising campaigns (unspecified).^{22,74} Several trials recruited through listservs, health plans, or survey panels.^{40,41,47,54,61,65,73,75–77} Other proactive recruitment sources included health facilities or clinics,^{44–48,51,58,60,74} quitlines,^{47,75} and worksites.⁵⁷ Several studies used a combination of recruitment strategies.

Participants

Average age in most studies was mid-30s to late 40s; four studies explicitly focused on young adults and recruited participants who were 18–30 years of age.^{40,61,76,78} The majority of studies enrolled a higher proportion of women; several trials recruited an equal number of men and women.^{64,69,70} Trials with a higher proportion of men^{46,51,53,55,57,58,68,76} recruited from sources where men were more likely to be represented (eg, workplace for operating engineers and human immuno-

deficiency virus [HIV] clinic). The only trial to enroll only women focused on cessation among pregnant smokers.⁵⁹ Approximately one-third of studies did not provide details about race; among those that did, the majority had primarily White participants. Some studies targeted specific racial or ethnic groups.^{55,64} Participants were most likely to have at least some college education; a majority of participants in three studies had a high school degree or less.^{39,51,57}

Intervention elements

The flexibility of the Internet allows for web-based cessation treatments to take myriad forms. In fact, this is one of the clearest findings from this review: there is currently no single or core web-based cessation treatment. The following groupings highlight common features among this diverse landscape.

Static web interventions: Ten trials^{22,37,44,45,50,53,62,68–70} included stand-alone static web components as part of the intervention condition. Static content was generally informational and non-tailored and contained content comparable to a printed cessation guide. Included in this category are static interventions in which the intervention is fully available and those that deliver intervention components over time. In some studies, static content was paired with additional features such as tailored feedback reports, text messaging, and/or social support.

Tailored feedback: Tailored feedback consists of advice or information provided to users based on responses to one or more assessments. Eight studies^{22,37,44,45,56,62,63,75} examined interventions consisting largely of a feedback report. Tailoring was often performed on the basis of participants' responses to an initial assessment and/or on the basis of participants' stage of quitting. The form of tailored messages, however, varied greatly. In the study by Wangberg et al,²² participants could receive up to 150 tailored emails over 6–12 months with tailoring on multiple factors. In contrast, Etter⁶³ provided participants with a single tailored letter, six to nine pages in length, based on a 62-item questionnaire.

Interactive/tailored web intervention: The majority of studies evaluated the effectiveness of interactive web interventions. Interactivity was defined as any part of a web intervention that solicited/required user input and included features such as exercises, quizzes, cost calculators, tailored messages, quit planning tools, training in coping strategies, and self-monitoring. A minority of the interactive interventions offered tailored content and/or guided users through the

intervention based on information provided by the participant (eg, as in the study by Wangberg et al).²²

Coaching analogs and social support: A number of trials included social support resources such as peers, coaches, or counselors. The most common form of social support was the provision of an asynchronous discussion forum. Eight trials^{22,37,44,45,53,67,68,77} included a discussion forum, either moderated by a peer or an expert, in at least some of the study arms. Seven trials included access to live coaching or counseling either via telephone, face-to-face counseling, or SMS text or email.^{38,48,52,57,66,77,78} Two studies evaluated other methods of accessing social support.^{40,56}

Other adjunctive components: Four trials described the use of SMS text messaging as part of the intervention.^{48,62,69,70} The two trials by Brendryen et al and Brendryen and Kraft^{69,70} also included interactive voice response calls. The studies by Muñoz et al^{37,68} and Leykin et al⁵³ included an online eight-module cognitive-behavioral mood management component in some arms. The study by Simmons et al⁷⁶ included videos and the ability to create video content.

Medication: Several studies provided pharmacotherapy along with the web-based intervention. Nicotine replacement therapy (NRT) was the most common form of pharmacotherapy and was included in seven trials.^{38,41,44,46,51,57,70} Medication treatment ranged from a 2-week starter kit used in the study by Fraser et al³⁸ to a 10-week starter kit used in the study by Strecher et al.⁴¹ Two trials^{47,58} included 12 weeks of varenicline. The study by Japuntich et al⁵² included a 9-week course of bupropion.

Comparison arms

Six studies involved a no-treatment control condition. The studies by Elfeddali et al⁶² and Haug et al⁴⁵ involved assessment-only control conditions. Smit et al³⁹ compared a fully automated, tailored Internet intervention to a no-treatment control. In a cluster randomized trial by Pisinger et al,⁶⁰ participants randomized to the control arm received usual care by their general practitioner. Swartz et al⁷³ tested a tailored, video-based Internet site in worksites against a waitlist control. Participants randomized to the control arm had access to the intervention after 90 days. Oenema et al⁶⁵ studied a multiple behavior change Internet intervention that addressed saturated fat intake, physical activity, and smoking. Smokers were encouraged to complete the smoking module first, which was interactive and included tailored feedback. Participants randomized to the control arm had access to the intervention after completing the posttreatment assessment at 1 month.

Five studies involved self-help print materials.^{44,51,55,69,70} Three studies compared largely static Internet interventions to self-help print materials, and two compared interactive Internet interventions to print materials. Emmons et al⁴⁴ adapted Partnership for Health-2, a smoking cessation intervention for cancer survivors, for delivery via the Internet and compared it to a print version of the program. The print arm received a series of manuals designed to be interactive (eg, worksheets and personalized content). McDonnell et al⁵⁵ compared a static website composed of six sequential sections with a printed version of the same program. Humfleet et al⁵¹ compared a static Internet intervention to a printed self-help guide among patients in an HIV clinic. Two studies by Brendryen et al and Brendryen and Kraft^{69,70} evaluated the effect of an interactive, multimodal (Internet, email, SMS, interactive voice response) cessation intervention against self-help print materials. All participants in the study by Brendryen and Kraft⁷⁰ received NRT.

Seven studies compared Internet interventions to face-to-face advice or counseling, either in individual or group format. The study by Dezee et al⁵⁸ involved in-person counseling (four 1.5-hour classes) and standard-dose varenicline. The control condition in the study by Japuntich et al⁵² consisted of 9 weeks of twice-daily bupropion sustained release, three brief individual counseling sessions, and five follow-up visits. In a cluster randomized trial conducted by Mehring et al⁴⁸ within primary care clinics, participants randomized to the control arm received usual care and advice from their practitioner. A pilot study by Shuter et al⁴⁶ among HIV clinic patients randomized participants in the control arm to standard care, defined as brief advice to quit and self-help brochure. All subjects were offered nicotine patches. An experimental study by Simmons et al⁷⁶ included a group-based intervention as one of the controls. In small groups, students reviewed paper versions of the content from the Internet intervention and discussed it during a group discussion. In the study by Humfleet et al,⁵¹ the control arm received six sessions of 40–60-minute in-person counseling plus NRT. In a cluster randomized trial by Pisinger et al,⁶⁰ general practitioners provided brief cessation counseling and referred smokers to five sessions of group-based counseling.

Two studies involved telephone counseling as a comparison condition.^{47,57} In the study by Choi et al,⁵⁷ participants were encouraged to call a toll-free telephone quitline and use NRT. A three-arm trial by Swan et al⁴⁷ compared proactive telephone counseling, an interactive website based on the same program, and a combined phone + Internet intervention. All participants received varenicline.

Twenty-three trials compared an interactive and/or tailored Internet intervention with a less intensive, static or generic Internet intervention.^{22,37,38,40,41,49,53,54,56,59,61,63,64,66–68,71,72,74–78} Two of these studies examined the active ingredients of an Internet intervention using a factorial design.^{41,54} The remainder of the trials employed two- or three-arm randomized designs to examine the comparative effectiveness of different Internet interventions.

Outcome measures

The primary endpoints differed widely among the studies, ranging from 1 or 2 months post randomization^{56,59,65} to 15 months post randomization.⁴⁴ Most studies used self-reported abstinence measures (ie, 7-day, 30-day abstinence) as the primary outcome abstinence metric. A small number of studies used more conservative metrics of self-reported abstinence.^{56,62,72,74} Humfleet et al,⁵¹ Japuntich et al,⁵² Shuter et al,⁴⁶ Simmons et al,⁷⁶ and Dezee et al⁵⁸ collected carbon monoxide samples; Mehring et al⁴⁸ collected urine cotinine; and Pisinger et al⁶⁰ confirmed smoking status via urine cotinine through mailed urine samples. In each of these trials, clinic-based or local recruitment/intervention made biochemical verification feasible.

Effects of interventions

Internet interventions compared to an assessment-only or waitlist control

Prior to analysis, we pooled the intervention arms used in the study by Elfeddali et al⁶² using data from Sample 1 as reported in the manuscript. We excluded the study by Oenema et al⁶⁵ from this analysis since the primary outcome was measured at 1 month post randomization and was based on self-reported abstinence in response to “Do you smoke?” We excluded the study by Pisinger et al⁶⁰ because of the low usage of Internet intervention. Pooled results from the four studies included Internet interventions (Figure 3) demonstrated a statistically significant effect in favor of the intervention (RR 1.60, 95% CI 1.15–2.21). However, results should be interpreted with caution as statistical heterogeneity was high ($I^2=51.7\%$). In addition, the study by Elfeddali et al⁶² was at high risk of attrition bias since follow-up attrition was higher in both intervention arms, though this likely resulted in an underestimate of the potential intervention effect under ITT analysis.

Static Internet interventions compared to self-help print materials

The study by Humfleet et al⁵¹ was excluded since we could not calculate ITT abstinence rates based on data presented in the

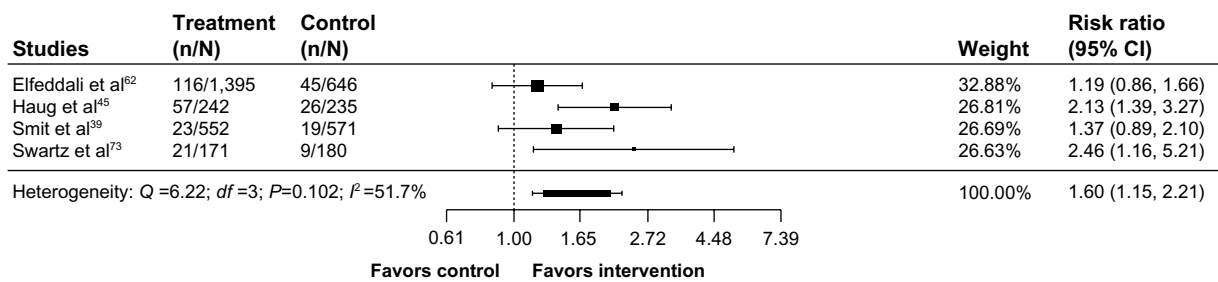


Figure 3 Internet interventions compared to assessment-only/waitlist control. **Abbreviation:** CI, confidence interval.

manuscript. Pooled results from the studies by Emmons et al⁴⁴ and McDonnell et al⁵⁵ (Figure 4) found a nonsignificant effect in favor of the print materials (RR 0.83, 95% CI 0.63–1.10). Both studies included in this analysis^{44,55} were at low risk of bias and had no statistical heterogeneity ($I^2=0\%$).

Interactive Internet interventions compared to self-help print materials

Pooled results from the two studies by Brendryen et al and Brendryen and Kraft^{69,70} (Figure 5) found a statistically significant effect in favor of the interactive Internet intervention (RR 2.10, 95% CI 1.25–3.52). Statistical heterogeneity was low ($I^2=41.6\%$), and both studies were at low risk of bias.

Internet interventions compared to face-to-face counseling

The study by Humfleet et al⁵¹ was excluded from this analysis since we could not calculate ITT abstinence rates based on data presented in the manuscript. The study by Pisinger et al⁶⁰ was excluded because of the low usage of the Internet intervention; only 15.8% of participants randomized to this arm accessed the program. The study by Mehring et al⁴⁸ was excluded because of the high risk of attrition bias: response rates were 85% and 59% for control and intervention, respectively. Pooled results from four studies^{46,52,58,76} (Figure 6) found a nonsignificant effect in favor of Internet interventions (RR 1.35, 95% CI 0.97–1.87, $I^2=0\%$).

Internet interventions compared to telephone counseling

Prior to the analysis, we combined the two arms from the study by Swan et al⁴⁷ that involved Internet treatment (Web, Phone + Web) and compared it to telephone counseling. Pooled results from the studies by Choi et al⁵⁷ and Swan et al⁴⁷ (Figure 7) found a nonsignificant effect in favor of telephone counseling (RR 0.95, 95% CI 0.79–1.13, $I^2=0\%$).

Internet interventions compared to other websites

Twenty-three trials compared Internet interventions to other web-based interventions. Excluded from this analysis were the studies by Bricker et al⁵⁰ and Berg et al⁶¹ (pilot studies focused on feasibility, no power analysis was conducted); Etter,⁶³ Herbec et al,⁵⁹ and Strecher et al⁵⁶ (primary outcome assessed at < 3 months); Leykin et al⁵³ (low rates of follow-up and high risk for attrition bias); Mañanes and Vallejo⁶⁴ (very low follow-up rates <5%); and Strecher et al⁴¹ (fractional factorial design precludes reporting of main effects). Pooled results for the remaining 15 trials (24 comparisons) found a significant effect in favor of Internet interventions compared to other websites (RR 1.16, 95% CI 1.03–1.31, $I^2=76.7\%$). The forest plot is presented in Figure 8. Two trials with college students in the study by An et al^{40,78} showed significant effects for the two experimental conditions over the control condition, and for a personally tailored website with peer coaching over the personally tailored website alone. In the

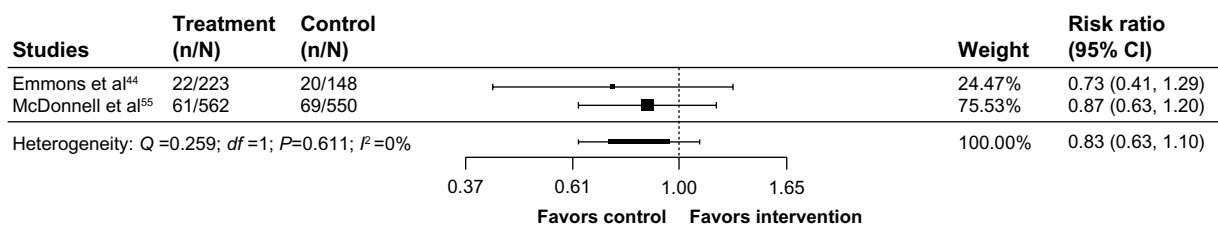


Figure 4 Static Internet interventions compared to self-help print materials. **Abbreviation:** CI, confidence interval.

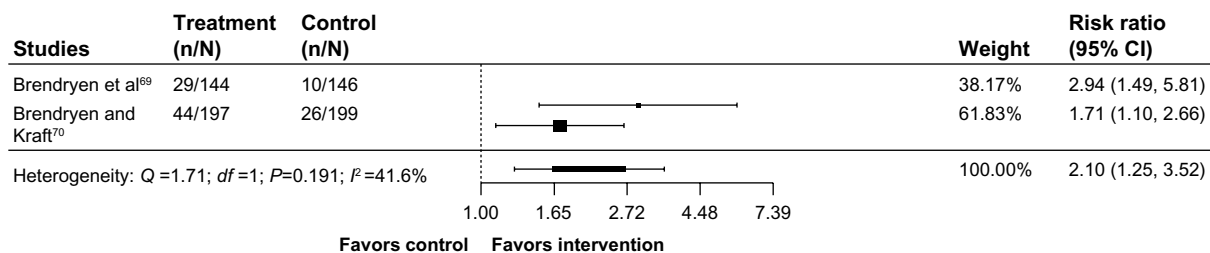


Figure 5 Interactive Internet interventions compared to self-help print materials.

Abbreviation: CI, confidence interval.

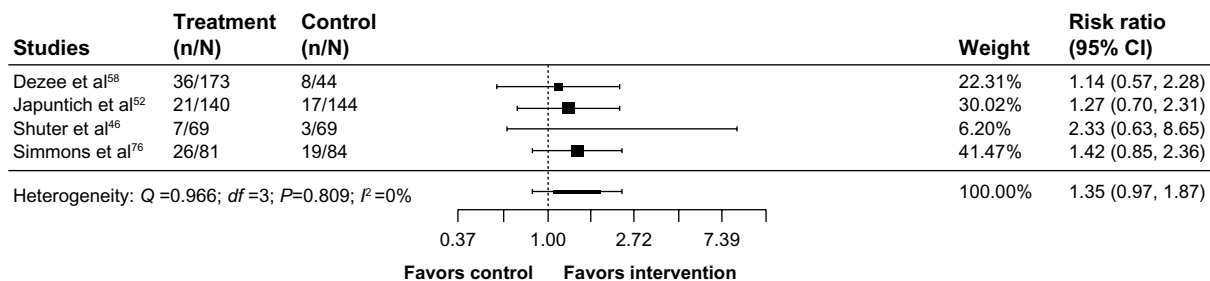


Figure 6 Internet interventions compared to face-to-face intervention.

Abbreviation: CI, confidence interval.

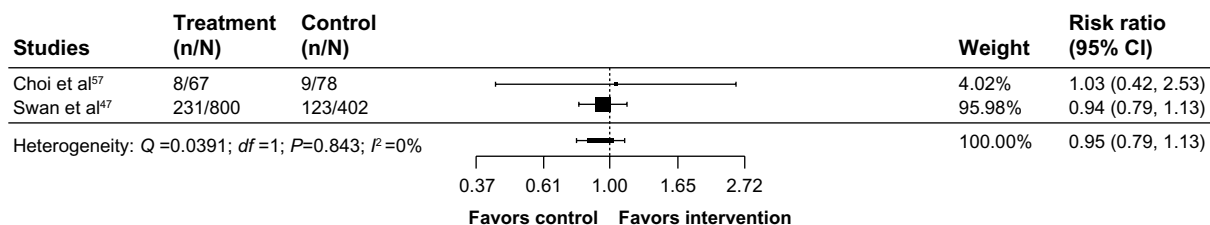


Figure 7 Internet interventions compared to telephone counseling.

Abbreviation: CI, confidence interval.

study by Stanczyk et al,⁷⁴ there was a significant effect of the computer-tailored video-based website over a static website with general information. Of the remaining 19 comparisons, eleven showed nonsignificant effects in favor of the experimental condition, with RRs at or below 1.34. In the study by McClure et al,⁵⁴ three of the four comparisons favored the more intensive/experimental factor over the control. Nonsignificant effects in favor of the control arm were observed in the studies by Graham et al,⁶⁶ Mason et al,⁷² McClure et al⁵⁴ (email factor), Muñoz et al⁶⁸ (static website + email vs static website), Muñoz et al³⁷ (study 3 and study 4), Stoddard et al,⁷⁷ and Wangberg et al.²²

Discussion

The goal of this systematic review was to evaluate the literature regarding the effectiveness of Internet cessation interventions, with particular reference to other

cessation interventions supported by treatment guidelines. We reviewed 40 randomized trials that included 98,530 participants published from January 1990 through April 2015. These studies varied considerably with regard to the intervention features, comparison conditions, participant characteristics, and cessation outcome. However, grouping studies by the nature of the comparison condition and by intervention type yielded the following findings: 1) Internet interventions outperformed assessment-only/waitlist controls, 2) largely static Internet interventions were equivalent to self-help print materials, 3) interactive Internet interventions outperformed self-help print materials, 4) Internet interventions appeared equivalent to counseling delivered via face-to-face and telephone interventions, and 5) Internet interventions outperformed a range of website controls, although statistical and clinical heterogeneity were high.

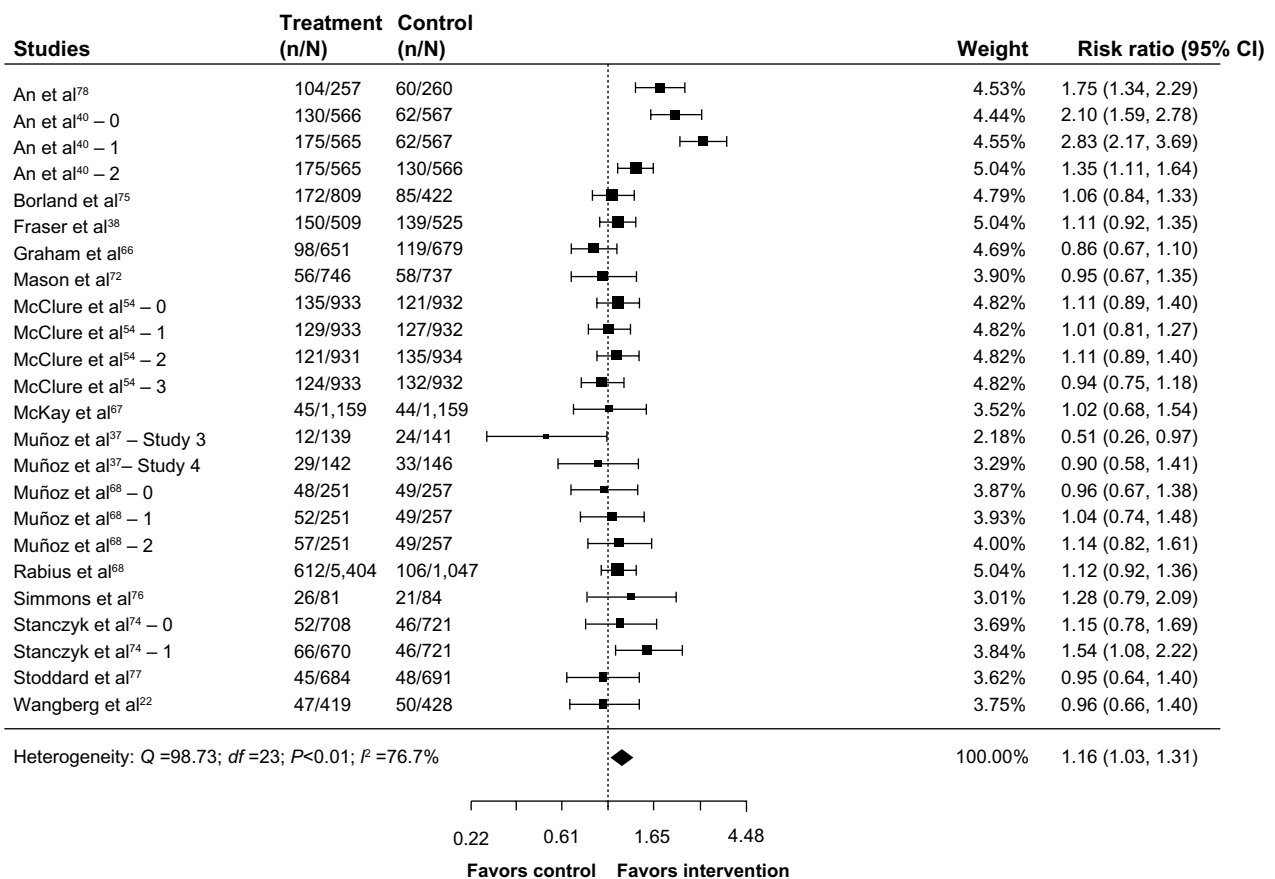


Figure 8 Internet interventions compared to other websites.

Notes: Comparisons are as follows: An et al⁴⁰: 0, personally tailored health information vs general lifestyle content; 1, personally tailored health information + peer coaching vs general lifestyle content; 2, personally tailored health information + peer coaching vs personally tailored health information. Fraser et al³⁸: Smokefree.gov vs “lite” version of website. McClure et al⁵⁴: 0, message tone (motivational/prescriptive); 1, testimonials (yes/no); 2, navigation (autonomous vs dictated); 3, email prompts (yes/no). Muñoz et al⁶⁸: 0, static website + email vs static website; 1, static website + email + mood management; 2, static website + email + mood management + bulletin board vs static website. Stanczyk et al⁷⁴: 0, tailored text-based website vs generic website; 1, tailored video-based website vs generic website.

Abbreviation: CI, confidence interval.

The finding that interactive Internet interventions outperformed print materials but largely static interventions did not is consistent with previous reviews,²⁷ with a larger number of studies included herein. Delivery of static content via the Internet may increase its reach, but engagement with static content online would be expected to be comparable to print content, which has not been shown to significantly increase abstinence rates.⁸ Self-assessments, self-monitoring, quitting-specific exercises, games, and social communications are now commonplace elements of online interactivity and are expected by end users. We note that the interventions included in these analyses were all published in the past 5 years, well past the advent of Web 2.0 social technologies and the proliferation of interactive components enabled by using JavaScript, Adobe Flash, and other languages that allow for a robust web experience. Results highlight the fact that the true potential of the Internet in promoting cessation is not exemplified by largely static interventions.

Our analyses did not detect significant differences between Internet interventions and face-to-face or telephone counseling. These findings are comparable to the results reported in the study by Civljak et al,²⁷ but with a larger number of trials. The studies of face-to-face counseling involved a range of counseling formats, including brief advice in the study by Shuter et al,⁴⁶ individual counseling in the study by Japuntich et al,⁵² and group interventions in the studies by Dezee et al⁵⁸ and Simmons et al.⁷⁶ Effect sizes favored Internet interventions in each of these comparisons, but did not reach statistical significance. In comparisons of Internet interventions with telephone counseling, Choi et al⁵⁷ found a nonsignificant effect in favor of the Internet intervention, whereas Swan et al⁴⁷ found a nonsignificant effect in favor of telephone counseling. The equivalence of Internet interventions to these approaches lends support to the notion that Internet interventions may belong alongside face-to-face and telephone counseling interventions in tobacco treatment guidelines.

The largest group of studies compared two or more Internet interventions. More than two-thirds of comparisons in this category favored the experimental condition, perhaps signaling significant progress in the development of modern, engaging, rigorous, and effective Internet cessation interventions. Identifying the active ingredients of Internet interventions is an important area for future research, yet only three studies used factorial designs to compare specific features in order to optimize the effectiveness of Internet interventions.^{38,41,54} Given the efficiency of this type of design and the speed with which it can advance the science of Internet interventions, more research of this type is needed.

Our results may not be as conservative as those reported in the study by Civljak et al.²⁷ Our use of the primary outcome specified in each trial rather than the longest available follow-up is methodologically sound given that many analyses of longer-term follow-up may have been underpowered; however, it could result in more optimistic, shorter-term outcomes than those presented elsewhere. In addition, our coverage of adherence and engagement is limited based on the nature and scope of this review. A large and growing number of studies point to engagement as a critical element in promoting abstinence.⁷⁹ We gathered information on engagement strategies for descriptive purposes but did not examine this as a moderating variable. Future reviews are encouraged to consider this important aspect of effectiveness.

Conclusion

In summary, based on this review of >10 years of research on Internet cessation interventions, the field has advanced significantly with newer interventions incorporating more interactive and engaging features. Six previous reviews have reported a mixture of conclusions, some more encouraging than others. Our goal was to address a practical question of relevance to payers and other decision makers regarding the role of Internet interventions in comprehensive tobacco control. As noted by the US Preventive Services Task Force,²⁶ “The best and most effective combinations [of cessation interventions] are those that are acceptable to and feasible for an individual patient.” Given the significant uptake of Internet interventions, their superiority to other broad reach cessation interventions (ie, print materials), and equivalence to other currently recommended treatment modes (telephone and in-person counseling), the results of this review suggest that Internet interventions have an important role to play in the arsenal of tobacco-dependence treatments.

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Disclosure

Amanda L Graham, Sarah Cha, and Megan A Jacobs are employees of Truth Initiative, a nonprofit public health foundation that runs BecomeAnEX.org, a web-based smoking cessation program. Kelly M Carpenter, Sam Cole, and Margaret Raskob are employees of Alere Wellbeing, a for-profit company that offers the Quit For Life comprehensive smoking cessation program which includes Web Coach®, a web-based smoking cessation intervention. Heather Cole-Lewis is an employee of Johnson & Johnson Health and Wellness Solutions, a for-profit company that offers Breathe®, a digital health coaching programs for smoking cessation. During the conduct of this study, Heather Cole-Lewis was an employee of ICF International which is a contractor to the National Cancer Institute (NCI) of the National Institutes of Health and supports Smokefree.gov, the NCI smoking cessation website. The authors report no other conflicts of interest in this work.

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